The effect of serial founder-flush cycles on quantitative genetic variation in the housefly

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Experimental populations of the housefly, initiated from a single outbred natural population, were subjected to five serial founder events of one, four, or 16 pairs of flies. After each bottleneck the populations were allowed to flush to approximately 1000 pairs, at which time they were assayed for additive genetic variance for eight morphometric traits using parental–offspring covariances. Additive genetic variance for all bottleneck sizes rose above the level of the outbred control in response to the first bottleneck and remained comparable to or higher than that of the control over most of the successive bottleneck episodes; no bottleneck size exhibited additive genetic variance significantly below the level of the control throughout the experiment. Such changes in additive genetic variance in response to bottlenecks are inconsistent with a model of neutral additive gene action, suggesting that non-additive components of genetic variance are likely to have affected the traits. Two models of non-additive genetic variance, pure dominance and additive-by-additive epistasis, provided reasonable fits to our data, but were not distinguishable from each other. Both empirical and theoretical results suggest that additive genetic variance for quantitative traits can remain high despite repeated reduction of the population size to as low as a single mated pair. Historical bottlenecks cannot be accurately inferred from levels of additive genetic variance for complex quantitative characters that are affected by non-additive components of genetic variance.

Keywords: bottlenecks, founder events, housefly, quantitative genetics.

Introduction

When the effects of individual loci affecting a quantitative trait combine in complete additivity, a population bottleneck is expected to decrease the genetic variance associated with the trait (Wright, 1951; Lande, 1980; Falconer, 1989). However, when the separate effects of individual alleles do not act in such a purely additive fashion, a population bottleneck may not lower additive genetic variance. For example, it has been shown theoretically that additive genetic variance can increase after a population bottleneck in the case of dominance among alleles within loci, even though the loci affecting the trait combine additively (Robertson, 1952; Cockerham & Tachida, 1988; Tachida & Cockerham, 1989a; Jiang & Cockerham, 1990). Moreover, theory has shown that interaction among individual loci (i.e. epistasis) can also result in increased additive genetic variance as the bottleneck causes a portion of the non-additive variance to be converted to the additive component (Cockerham & Tachida, 1988; Goodnight, 1987, 1988; Tachida & Cockerham, 1989b).

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The degree to which quantitative traits are affected by non-additive genetic processes is largely unknown. The widespread occurrence of inbreeding depression implicates directional dominance for viability and reproductive traits (Robertson, 1955; Crow & Kimura, 1970; Charlesworth & Charlesworth, 1987; Falconer, 1989); however, evidence for epistasis affecting quantitative traits is less compelling (see reviews by Barker, 1974, 1979; Barton & Turelli, 1989; Cohan *et al.*, 1989; Geiger, 1988), although the theoretical likelihood of epistasis is high for fitness traits under stabilizing selection (Robertson, 1955; Wright, 1965, 1969, 1977). When epistatic interactions are found, they are often not large relative to the additive genetic component (e.g. Kearsey & Kojima, 1967; Shrimpton & Robertson, 1988a,b; Barnes et al. 1989; Paterson *et al.*, 1990).

One approach to detecting non-additive effects is to subject experimental populations to inbreeding and/or bottleneck regimes to estimate changes in the additive component of variance (or heritability) relative to neutral expectation. Several cases with apparent increases in the additive genetic variance of inbred and/or bottleneck lines have been reported. Lopez-

Fanjul & Villaverde (1989) found an average increase in the genetic variance associated with viability within and among lines of *D. melanogaster* subjected to full-sib mating. Abplanalp (1988) suggested that non-additive effects were responsible for increased genetic variance of egg production within inbred lines of white leghorn chickens. Increased heritability for sterno-pleural bristle number was reported by Lints & Bourgois (1982) for a line of *D. melanogaster* that had undergone an accidental bottleneck, and Carson & Wisotzkey (1989) found increased karyotypic variance in a population of *D. silvestris* that had been reduced to six individuals. Polans & Allard (1989) reported increased coefficients of (phenotypic) variance for five life-history traits in the ryegrass, *Lolium multiflorum*, which had been subjected to experimental bottlenecks.

In an experiment to investigate the effects of experimental founder-flush of three sizes (one, four, and 16 pairs) in the housefly, we observed increases in the additive component of variance for eight morphological traits estimated from parental–offspring covariances (Bryant *et al.*, 1986). Moreover, all 12 bottleneck lines had higher average additive genetic variance relative to neutral expectation (χ^2 for 1:1 expectation around neutral expectation = 12.0; $P < 0.001$), providing clear evidence that additive genetic variance for quantitative traits can increase following a single founder-flush cycle. Of these experimental lines, two lines for each bottleneck size were carried through four additional founder-flush cycles with assays for additive genetic variance after each flush phase. Because the minimum level of inbreeding after five serial bottlenecks is a 10-fold difference between the single-pair and 16-pair lines, these data should provide a more powerful assessment of the effect of inbreeding on additive genetic variance than did the single bottleneck episode evaluated previously. Specifically, we document changes in additive genetic variance over the course of five serial bottlenecks and compare the observed changes in additive genetic variance with patterns predicted from models of additive, dominance, and epistatic genetic variance. Patterns of divergence in phenotypic means among lines are evaluated in a separate paper (E. H. Bryant & L. M. Meffert, unpublished observations). These are the first such empirical data investigating the effects of multiple bottlenecks on quantitative genetic variation.

Materials and methods

A single large sample of an outbred population of houseflies was taken from a landfill population at Alvin, TX. After establishment in the laboratory, bottleneck lines were initiated using the offspring from either one, four, or 16 pairs of flies. By combining progeny from isolated male–female pairs, the number of founders was exactly determined. The bottleneck populations were allowed to flush to normal laboratory size (approximately 1000 pairs), taking about five generations. Four replicate lines were established for each bottleneck size for the first bottleneck, and two of these lines per bottleneck size treatment were subjected to an additional four founder-flush cycles, giving a total of five serial bottleneck episodes per line. The control (base population) line was maintained in the laboratory throughout the course of the experiment at approximately 1000 pairs.

After each population flush, additive genetic variances for eight morphometric traits in the bottleneck and control lines were separately estimated as the average of sire, dam, and midparental-offspring covariance of log-transformed measurements taken with an ocular micrometer. Negative variance estimates were set to zero. As these negative values occurred more often in the control, due to it having the lowest genetic variance across the experiment, tests of differences between bottleneck lines and control are conservative. The eight morphometric traits were (for a full description of traits, see Bryant, 1977): wing length, wing width, head width, inner-eye separation, scutellum length, scutellum width, thoracic suture length, and metafemur length. The separate estimates of additive genetic variance for the eight traits were averaged over traits within each line and bottleneck episode. The estimates for the two replicate lines within a bottleneck size were then averaged, weighting each by the number of families used to obtain the estimate, to obtain a single estimate of additive genetic variance for each bottleneck size treatment over the five cycles. The parents and three female offspring were measured per family; the average numbers of families used for each replicate line and bottleneck episode were 28, 29, 35, and 36 for the single-pair, four-pair, 16-pair, and control, respectively. All flies for quantitative genetic variation estimates were reared under optimal densities of 80 eggs/18 g CSMA larval medium at 27°C to control for the effects of larval density and temperature on size. For convenience all resulting variance estimates were multiplied by 10^4.

Results

Quantitative genetic estimates

In order to compare additive genetic variances for bottleneck and control lines over the serial bottlenecks the control line was first examined for possible monotonic changes through the duration of the experi-

ment. The six successive estimates for the average additive genetic variance for the control and the linear regression of these values onto bottleneck episode number are shown in Fig. 1. Average additive genetic variance for the control was significantly greater than zero ($P < 0.05$) but showed no significant linear change over the 33 generations of the experiment ($P > 0.05$). As there was no linear trend in the control, and the number of families was approximately the same among lines, the separate estimates over the six sampling periods can then be combined into a single mean (and variance) estimate for the control, to be compared with the corresponding estimates for the bottleneck treatments; this procedure is essentially equivalent to an experimental bootstrap (e.g. see Efron, 1982; Efron & Gong, 1983).

The estimates for the additive genetic variances averaged over the two replicate lines for each bottleneck size and the expected decline in variability, based on purely additive effects [i.e. a loss of $1/(2n)$ per bottleneck episode from the average control value, where n is the number of founders], are given in Fig. 2, along with the 95 per cent upper confidence bounds to this neutral expectation. All three bottleneck sizes exhibited levels of additive genetic variance above the control and significantly greater than neutral expectation for at least some of the bottleneck episodes (5 of 5 for the single-pair; 2 of 5 for the four-pair; 4 of 5 for the 16-pair, Fig. 2). Additionally, no bottleneck line had significantly lower additive genetic variance than the control during the entire course of the experiment (lower 95 per cent confidence limit for additive genetic variance = 2.39). Hence, not only were the additive genetic variances for bottleneck lines after the first bottleneck episode higher than predicted from neutral

theory, as we previously reported, but they remained comparable to or higher than the control throughout the additional four founder-flush cycles.

Effects of non-additive components of variance

The neutral additive model appears inadequate to explain our results, so models incorporating non-additive components of variance are warranted. The effect of directional dominance on additive genetic variance after a single bottleneck was addressed in a prior study (Bryant et al., 1986), and we extend the model here to include serial bottlenecks. Briefly, we assume that the loci affecting a trait act independently (i.e. exhibit no epistasis), each with complete dominance between two alleles. The additive genetic variance for the ith locus is then $V_A(i) = 8pq^3a^2$, where q is the frequency of the recessive allele $(p = 1 - q)$ and a is the average effect of an allelic substitution on the trait (Falconer, 1989). The expected additive genetic variance contributed by a locus is the average of the additive genetic variances for all possible allele frequencies, weighted by their binomial probabilities of occurrence after a bottleneck, so that $V_A = \Sigma V_A(i) \times Pr(p_i)$ is the probability of the recessive allele being p_i based on binomial expansion. No further changes in allele frequencies are assumed through each flush phase, so each successive bottleneck is based on the allelic frequency distribution of the previous bottleneck. Assuming that the initial frequencies of recessive alleles at all loci affecting the trait are approximately equal, the distribution of interlocus effects is identical to the expected distribution of effects within a single locus, so V_A is also the expected additive genetic variance after a bottleneck averaged over all loci.
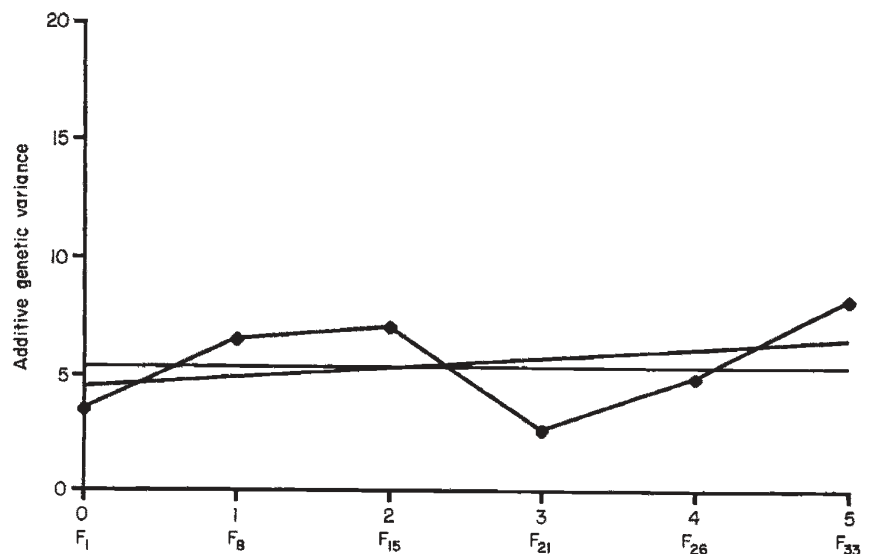

Fig. 1 Additive genetic variance (averaged over eight traits) for the outbred control over the six sampling periods of the experiment. Linear regression of additive genetic variances onto sampling time is shown, along with the average value for the control (horizontal line, average = 5.40). $y = 4.3848 + 0.40764x; r = 0.36$.
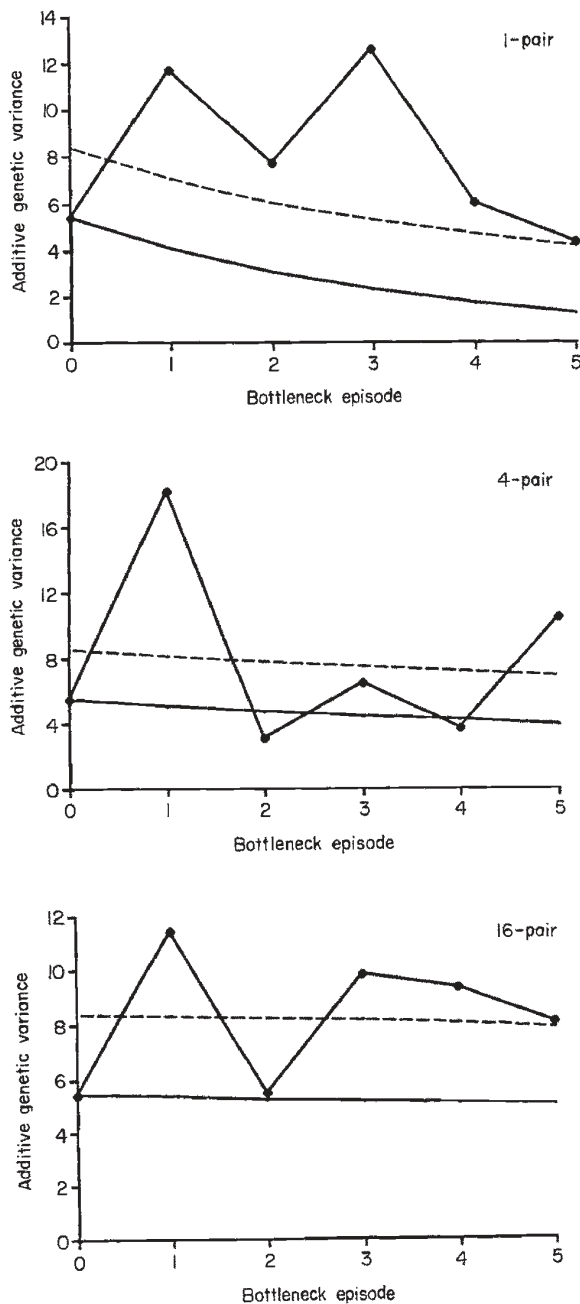
Fig. 2 Additive genetic variances for the three bottleneck sizes over the five bottleneck episodes. Expected values (———) and 95 per cent upper confidence bounds (— — —) under the neutral additive model are shown, based on average additive genetic variance of the control.

An approach to studying the effects of epistatic interaction on additive genetic variances in bottle-necked populations was provided by Goodnight (1987, 1988), using the co-ancestry and drift models developed by Cockerham (1967), Cockerham & Weir (1973) and Weir & Cockerham (1973). To simulate our

estimates of additive genetic variance, taken after a period of population flush following each bottleneck episode, we used the rates of conversion of non-additive to additive genetic variance for free recombination, as suggested by Goodnight (1988). For each successive bottleneck, the current level of additive genetic variance was decremented by the expected neutral rate of $1/(2n)$ and, as well, incremented by the conversion of non-additive to additive genetic variance, the net result of these two processes being the new value for additive genetic variance. The rates of conversion of non-additive to additive genetic variance during each bottleneck episode from Goodnight (1988 and personal communication) were 75.0 per cent, 23.4 per cent and 6.2 per cent for the single-, four-, and 16-pair bottleneck sizes, respectively. Conversely, the percentage of the non-additive variance retained after each successive bottleneck was 56.25 per cent, 87.8 per cent and 96.97 per cent, for the single-, four-, and 16-pair lines, respectively.

Without selection, additive genetic variance in either non-additive model would increase with up to nearly 50 per cent inbreeding, depending upon the initial magnitude of dominance or epistatic variance in the ancestral population. To account for apparent declines in additive genetic variance with lower inbreeding levels, and to generalize the basic models, we incorporated selection into both non-additive models. For the dominance model we assumed selection against the recessive homozygote during the flush phase, so the decrease in frequency of the recessive allele at each locus was taken to be $\Delta q = -sq^2 p$ per generation, where s is the selection coefficient against homozygous recessives with frequency q^2 (Falconer, 1989). In the epistatic model, selection acted directly against the component of additive genetic variance as an overall percentage decrement in additive genetic variance during the entire flush phase. In both models, selection was applied for the five generations of each population flush following each successive bottleneck. The parameters varied were: initial frequency of recessive alleles (dominance model), the initial percentage of non-additive genetic variance (epistatic model) and the intensity of selection (both models). Expected changes in additive genetic variance were calculated for five serial founder-flush cycles, and a response surface was fitted to the resultant additive genetic variances using the distance-weighted least-squares smoothing methods of SYGRAPH (SYSTAT, Inc., Evanston, IL, U.S.A.).

Figures 3a–3c and 4a–4c show the response surfaces of additive genetic variance for the dominance model and the epistatic model, respectively, for the five bottleneck episodes and three bottleneck sizes. The two initial allele frequencies of $q = 0.1$ (upper
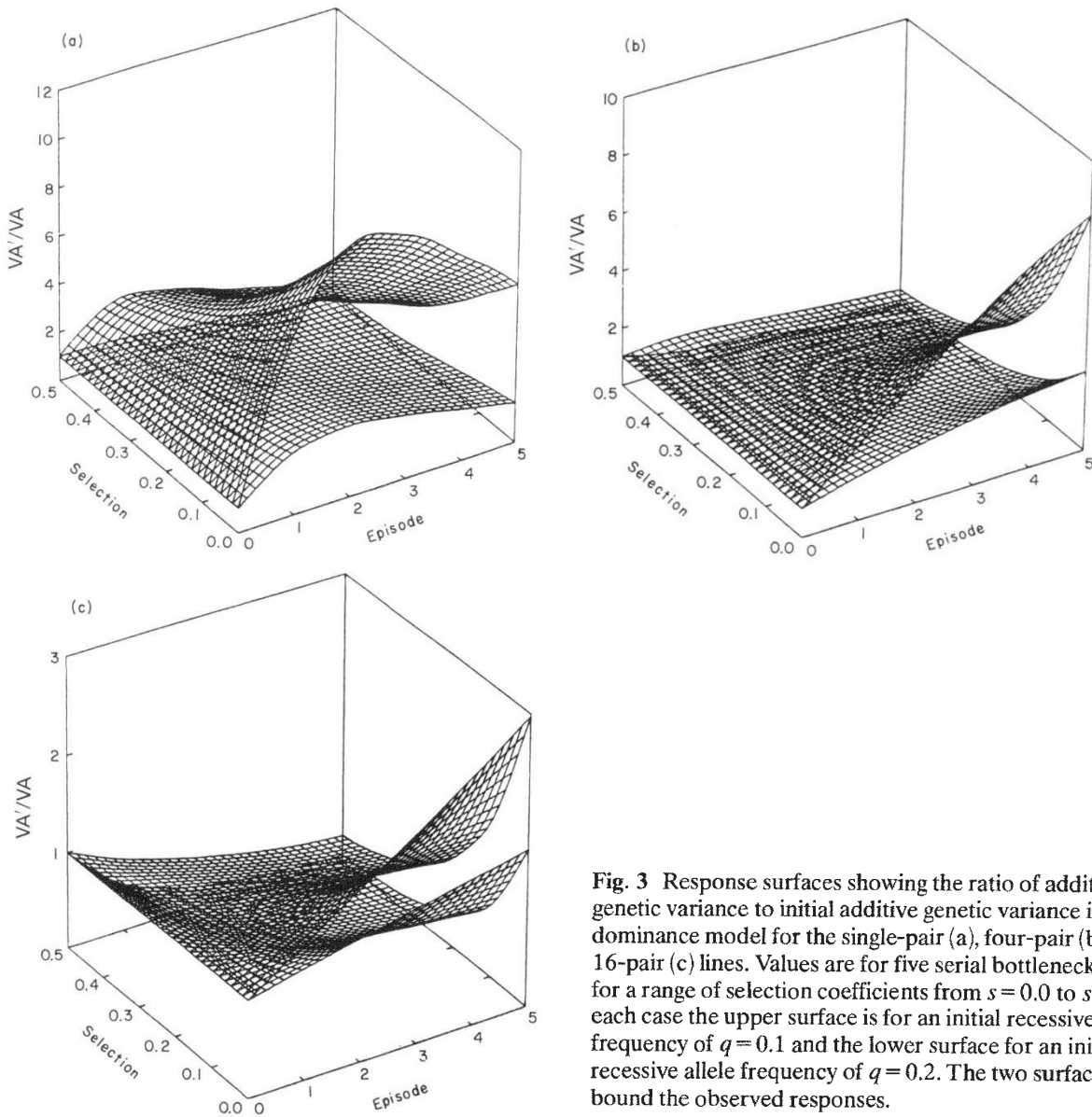
Fig. 3 Response surfaces showing the ratio of additive genetic variance to initial additive genetic variance in the dominance model for the single-pair (a), four-pair (b), and 16-pair (c) lines. Values are for five serial bottleneck episodes for a range of selection coefficients from $s = 0.0$ to $s = 0.5$. In each case the upper surface is for an initial recessive allele frequency of $q = 0.1$ and the lower surface for an initial recessive allele frequency of $q = 0.2$. The two surfaces bound the observed responses.

curve) and $q = 0.2$ (lower curve) (dominance model) and initial levels of non-additive genetic variance of 75 per cent (upper curve) and 60 per cent (lower curve) (epistatic model), over a range of selection coefficients $(s = 0.0$ to $s = 0.5)$ are shown for each model. These parameter ranges were chosen from among a larger set modelled because the response surfaces bracketed the observed additive genetic variances. In the dominance model without selection, additive genetic variance increases for the single pair lines until the third bottleneck, while for the larger bottleneck sizes additive genetic variance increases through all five bottlenecks. With increasing selection, additive genetic variance for all three bottlenecks sizes initially rises and then begins to decrease in later bottlenecks. The epistatic model

showed a very similar response in additive genetic variance for the three bottleneck sizes.

To identify which parameter conditions fit the data best, an overall least-squares fit of the observed additive genetic variances to those predicted by the models was computed for each set of parameters and summed over the three bottleneck sizes. The best fit for the dominance model occurred with an initial recessive allele frequency (q) of 0.2 and selection (s) of 0.1, yielding a least-squares value of 11.37. The best overall least-squares fit of the data to the epistatic model occurred with an initial non-additive genetic variance of 60 per cent and no selection, yielding a least-squares value of 9.48, which was slightly better than that for the dominance model. Both models, however, fitted the data
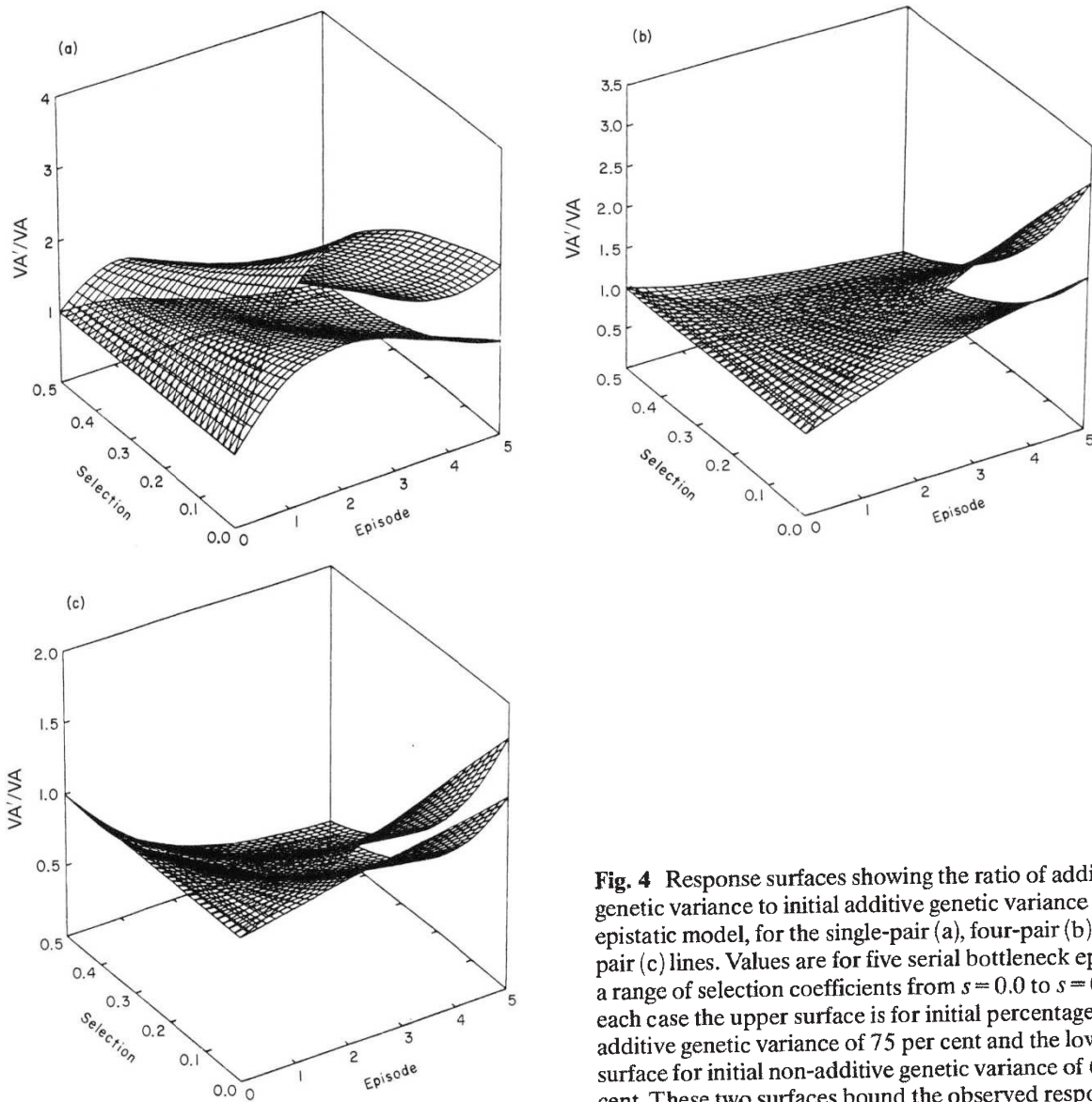
Fig. 4 Response surfaces showing the ratio of additive genetic variance to initial additive genetic variance in the epistatic model, for the single-pair (a), four-pair (b), and 16-pair (c) lines. Values are for five serial bottleneck episodes for a range of selection coefficients from $s = 0.0$ to $s = 0.5$. In each case the upper surface is for initial percentage of non-additive genetic variance of 75 per cent and the lower surface for initial non-additive genetic variance of 60 per cent. These two surfaces bound the observed responses.

considerably better than the neutral model, which yielded a least squares fit of 18.55.

Discussion

Non-additive genetic processes must have structured our initial trait variances because the data clearly do not fit neutral additive expectation by exhibiting increased rather than decreased additive genetic variance following an initial bottleneck. As electrophoretic variation for these same lines largely conformed to neutral expectation by exhibiting continued losses in both the average heterozygosity and number of alleles over the five bottlenecks, in accordance with bottleneck size (McCommas & Bryant, 1990), the

increased levels for additive genetic variances were not attributable to accidental inter-line contamination. Nor were the populations large enough for sustained periods of time (flushes averaged approximately five generations) to make mutation a likely source of new variation, even with the high mutation rate reported for quantitative traits (e.g. Lande, 1976; Lynch, 1985). The initial increase in additive genetic variance persisted for most lines despite the intervention of subsequent bottlenecks; therefore, the level of additive genetic variance for morphometric traits in relation to a known ancestor is a poor indicator of historical bottlenecks.

While the model of Goodnight (1988) incorporating additive-by-additive epistasis fitted our data slightly better than did the pure dominance model, it is clearly diffi-

cult to differentiate between these possible effects, based on a least-squares fit alone. Our models only contrasted each non-additive genetic process in the absence of the other, and thus it would be far more difficult to dissect out separate processes if both dominance and epistasis affected the traits.

In testing for differences in additive genetic variance between bottleneck lines and the control, we employed the variance of repeated measures from the control. This is satisfactory as long as the variance of bottleneck lines was not greater than that of the control. Even though the effects of linkage are minimized by the flush (Avery & Hill, 1977; Cockerham & Tachida, 1988; Cockerham & Weir, 1983), the variance among bottleneck lines could still be inflated by the initial sampling of founders (Lynch, 1988). Lynch (1988) predicted that the coefficients of variation among replicate lines after a single bottleneck, based on founder size alone, for the three bottleneck sizes of our protocol, would be 0.50, 0.25, and 0.12, for the single-, four-, and 16-pair lines, respectively. In contrast, these coefficients of variation were 0.33, 0.36, and 0.29, respectively. As the coefficient of variation from resampling the control line was 0.40, every bottleneck treatment had a lower coefficient of variation than the control (none was significantly different from the control; $P > 0.05$). Moreover, the coefficient of variation for the single-pair lines should be four times greater than that for the 16-pair lines, but the high congruence of among line coefficients of variation supports our basis for significance testing and suggests that neither linkage nor initial sampling of founders significantly affected our analyses. Because the near concordance of coefficients of variation among bottleneck treatments and control suggested that additive genetic variance may be log-normally distributed (Bryant, 1986), the tests in Fig. 2 were repeated using log-transformed additive genetic variances with nearly identical outcomes, so non-normality of additive genetic variances did not apparently prejudice our analyses.

Because additive genetic variance for fitness-related traits is generally regarded as an indicator of evolutionary potential, at least in the short term (Fisher, 1958), bottlenecks have generally been assumed to lower the rate of evolutionary change (e.g. Barton & Charlesworth, 1984; Charlesworth & Smith, 1982). However, our bottleneck populations may not have sacrificed much of their evolutionary potential, even when subjected to repeated single-pair bottlenecks, in that they retained much of the additive genetic variance present in the outbred population. While our morphometric traits are not components of fitness *per se*, they are likely to be related to fitness through a correlation with general body size (e.g. Bryant *et al.*, 1986), so

sufficient additive genetic variance for components of fitness also may have remained in these bottleneck populations. This is supported by parallel data on fitness components for these same lines reported by Bryant *et al.* (1990) and Meffert & Bryant (1991), who showed that by the end of the experiment most bottleneck lines were as fit as the outbred control despite being significantly lower in these fitness components after the first bottleneck (Bryant *et al.*, 1986). The issue as to whether or not bottlenecks seriously erode evolutionary potential remains moot; consequently, inferences as to whether historical bottlenecks had occurred will not be accurate using genetic variances for quantitative traits.

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